REMARKS

Claims 59-87 are pending in the application. Claims 62 and 66-87 have been withdrawn from further consideration as being drawn to non-elected inventions. Claims 59-61 and 63-65 are under examination. Applicant acknowledges the Examiner's renumbering of the claims and has duly incorporated the Examiner's amendment in the pending claims. To properly reflect changes in claim numbering, the claim dependencies have been amended.

Claim 59 has been amended to describe the inherent characteristics of the fusion polypeptide. Claims 59, 63, 67, 75, and 79 have been amended to recite a vector comprising a "nucleotide sequence . . ." Support is found throughout the specification, for example on page 23. In Claims 59 and 71-74, the term "domain" has replaced the word "motif." Support is found at least on page on page 8, lines 23-26. Claims 61, 62, 69, 70, and 78 have been amended to recite proper antecedent basis in light of the amendment of Claim 59. Lastly, the specification has been amended where appropriate to correct obvious errors. Applicant submits that no new matter is entered by way of the foregoing amendments.

Applicant requests reconsideration of the rejections in view of the following comments with respect to the claims under examination.

Restriction and Withdrawal of Claims

The Examiner has withdrawn Claims 62 and 66-87 from further consideration on the merits because there is no allowable generic or linking claim. Applicant emphasizes that Claims 60-87 ultimately depend from Claim 59. Consequently, should Claim 59 be found allowable, the Examiner is requested to rejoin the withdrawn claims and examine these claims for patentability during prosecution of this case. See MPEP § 809 and § 809.02(c). Applicant also emphasizes that he is entitled to consideration of additional species upon an indication that the generic claim is allowable. See MPEP § 809.02(c).

Objections in the Specification

The specification is objected to under MPEP § 608.01 for having an embedded hyperlink on page 9, line 25.

Applicant has amended the paragraph, deleting portions of the hyperlink to disable its recognition as a HTML code. Applicant believes that the amendment places the application

in compliance with PTO practice and MPEP § 608.01. Accordingly, Applicant requests withdrawal of the objection.

The specification is also objected to for various typographical errors. In response, Applicant has made an effort to correct obvious typographical and grammatical errors where found in the specification.

Amended Abstract

The abstract has been amended to conform to the guidelines as provided in MPEP § 608.01(b). The newly submitted abstract is consistent with the content of the technical disclosure. Accordingly, entry of the amended abstract is requested.

Rejections Under 35 U.S.C. § 112, first paragraph: Written Description

Claims 59-61 and 63-65 stand rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement. The Examiner alleges that the specification lacks sufficient description of the claimed retroviral vectors. Applicant traverses the rejection.

A person of skill in the art reading the disclosure would clearly conclude that Applicant was in possession of the claimed subject matter. For instance, the specification specifically describes the claimed retroviral vectors on page 24, lines 1-2 and 7. Moreover, the Examiner is directed to Figure 15A, which provides a cartoon of a "Retroviral library construct." The illustration shows a fusion nucleic acid with LTRs, also known as "long terminal repeats," on the left and right ends of the fusion nucleic acid. LTRs are well-known elements of retroviral vectors. Proceeding from the left to the right of the cartoon illustration, the construct contains a nucleic acid region encoding IntB, a nucleic acid region encoding a peptide of variable amino acid residues X_2 to X_8, and a nucleic acid region encoding Int A. Two specific amino acid sequences of interest, RGD7 (SRGDGWS) and RGD9 (SGRGDGWGS), are indicated. A fluorescent reporter gene encoding green fluorescent protein (*i.e.*, GFP) is used as a reporter for protein expression.

The Examiner is also directed to the original claims, which may serve as a basis for satisfying the written description requirement. See MPEP § 2163. Original Claim 10 refers to a fusion nucleic acid encoding a C-terminal intein motif, a peptide, and a N-terminal intein motif. Original Claim 11, which depends from Claim 10, recites that the fusion nucleic acid

is in the form of a retroviral vector. It is clear that all of the identifying characteristics of the presently claimed retroviral vectors were described in the original claims.

As supported by the descriptions in the specification, drawings, and original claims, the disclosure describes all limitations of the claimed retroviral vectors in sufficiently complete form such that a person skilled in the art would clearly recognize that the Applicant was in possession of the claimed subject matter. Accordingly, withdrawal of the rejection is requested.

Rejections Under 35 U.S.C. §112, second paragraph

Claims 59-61 and 63-65 stand rejected under 35 U.S.C. § 112, second paragraph for indefiniteness.

Specifically, Claim 59 is rejected as being indefinite in regards to phrases and terms "a first region", "capable", "generating" and "motif." Applicant traverses the rejection.

In regards to the phrase "first region", a person of ordinary skill in the art reading the claims in light of the specification would find the term precise and definite. However, in the interests of expediting prosecution of this case, the claim has been amended to recite a "nucleotide sequence," which describes what is inherent in the claimed vectors. In view of the amendment, withdrawal of the rejection is requested.

In regards to the phrase "capable of generating," the phrase describes with requisite precision and clarity the inherent properties of the fusion polypeptide encoded by the claimed nuclei acid. The encoded linear peptide is capable of generating a cyclic peptide via a cyclization reaction mediated by the intein domains, as clearly pointed out in the specification and the figures (see, *e.g.*, Figures 1 and 2). Applicant has amended the claim to restate this cyclization reaction displayed by the fusion polypeptide. Withdrawal of the rejection is requested.

In regards to the term "motif," the term has been amended to "domain." Support is found at least on page 8, lines 23-26. The amendment merely restates the term as provided in the specification. In view of the amendment, withdrawal of the rejection is requested.

Claim 60 is rejected for lack of clarity with respect to "altered" splicing activity. Applicant traverses the rejection.

The specification on page 32, lines 7-15 provides the following description:

> By "altered" cyclization activity" refers to any characteristic or attribute of an intein that can be selected or detected and compared to the corresponding property of a naturally occurring intein. These properties include cyclization efficiency, stability, etc. Cyclization efficiency may be affected by the presence or absence of a given amino acid, the size of the peptide library, etc. Unless otherwise specified, altered" cyclization activity, when comparing the cyclization efficiency of a mutant intein to the cyclization efficiency of wild-type or naturally occurring intein, is preferably at least 1-fold, more preferably at least a 10-fold increase in activity.

Applicant submits that the term is well delineated and is clear to those skilled in the art. Accordingly, Applicant requests withdrawal of the rejection.

Claim 61 is rejected for lack of antecedent basis for "random peptide." The Examiner appears to suggest that Claim 59 does not clearly distinguish between the various peptide forms encoded by the vector. Applicant traverses the rejection.

The language of Claim 59 clearly differentiates between the peptide entities in the claim, *i.e.*, fusion polypeptide, cyclic peptide, and a peptide, such that a reference to "the peptide is a random peptide" in Claim 61 has sufficient antecedent basis to satisfy § 112, second paragraph. However, in an effort to improve form of the claims for prosecution, "a peptide" has been revised to "a peptide of interest." Accordingly, withdrawal of the rejection is requested.

Claim 63 is rejected as being indefinite for the phrase "second region." The Examiner alleges that it is not clear whether the second region is separately encoded or part of the fusion polypeptide. Applicant traverses the rejection.

The phrase is clear and precise to those skilled in the art given the descriptions of various uses of reporter genes (*e.g.*, expression monitoring, cell selection, detection of cyclic peptide formation, etc.) provided in the disclosure and the considerable knowledge in the art with respect to reporter genes. However, for consistency with the amendment described above for "first region", the claim has been rephrased in the context of a "nucleotide sequence." Accordingly, Applicant requests withdrawal of the rejection.

Rejections Under 35 U.S.C. § 102(a)

Claims 59-61 and 63 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Scott, C.P., *Proc. Natl. Acad. Sci. USA* 96:13638-13643 (1999). Claims 59-60 and 63 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Iwai, H. et al., *FEBS Lett* 459:166-

172 (1999). Claims 59-61 and 63 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Evans, T.C., *J Biol. Chem.* 274:18359-18363 (1999). Applicant traverses the rejection.

All of the cited references (*i.e.*, Scott, Iwai, and Evans) are directed to expression of intein-containing proteins in bacterial cells using bacterial expression vectors. For instance, Scott uses bacterial plasmid pDIMC7 as the base vector for constructing intein expression plasmids and expresses inteins in *E. coli.* strain XL-1 Blue. Iwai and Evans use bacterial vector pTYB2 as the base vector for constructing the expression plasmids and express inteins in *E. coli.* strain ER2566. Thus, the teachings of Scott, Iwai, and Evans are focused on producing cyclic peptides in bacterial systems, where inteins are naturally expressed.

In contrast, the presently claimed subject matter is drawn to eukaryotic expression vectors based on retroviral vectors specifically designed to express the recited fusion polypeptides in eukaryotic cells. Retroviruses typically infect mammalian cells and depend on the eukaryotic cellular machinery for expression of viral proteins and replication of viral particles. Exemplary mammalian cells suitable for use with the claimed retroviral vectors are expressly provided in the specification from page 29, line 24 to page 30, line 5. In comparison to the instant application, the references cited in the Office Action are completely deficient in any teaching or suggestion for the use of retroviral constructs to produce cyclic peptides in eukaryotic cells. Accordingly, the cited references do not teach or suggest each and every element of the claims as required to anticipate the claimed subject matter.

In view of the foregoing, Applicant requests withdrawal of the rejections under 35 U.S.C § 102(a).

CONCLUSIONS

Applicant submits that Claims 59-61 and 63-65 satisfy all of the statutory requirements for patentability and are in condition for allowance. An early notification of the same is kindly solicited. If upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to direct any calls in connection with this application to the undersigned at (650) 494-8700.

No fees beyond those included with the Amendment are believed due. However, the Commissioner is authorized to charge any additional required fees, or credit any

overpayment, to Dorsey & Whitney LLP Deposit Account No. 50-2319 (Our Order No. A-68614-1 (467802-00204)/AMP/CYO).

Respectfully submitted,

DORSEY & WHITNEY, LLP

Dated: October 21, 2003

By: _____

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